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# A STUDY ON THE DETERIORATION OF MORPHINE IN THE FRESH LATEX OF PAPAVER SOMNIFERUM L.

Part I

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## INTRODUCTION

Opium is traditionally collected in India by making incisions (lancing) in capsules of Papaver somniferum during the afternoon hours and scraping off the air dried latex (opium) from the capsule surface the next morning. There is an interval of 12 to 16 hours from the time of lancing to the collection of opium. Normally 3 to 4 lancings, each lancing being done at an interval of 72 hours, are carried out to obtain the maximum quantity of latex. The composite of opium of all lancings from each cultivator is transported to the Government factories where it is analysed for morphine content. Normally there is a time lag of more than a month between the collection of opium and the actual estimation of morphine. Atmospheric day temperatures during summer months (March to May) vary from 32°C to 40°C when the opium is exposed to sun and hot air, before and during collection, on farm storage and transport to the factory. These factors may result in the deterioration of morphine in fresh latex.

As early as 1935, Troshohenko et al. (1) pointed out that the fresh latex, immediately after lancing, contained 20% morphine on dry basis compared to 10 to 13% in opium following collection and storage. Fulton (2) in his publication on "The Opium Poppy and Other Poppies" has also reported similar findings. According to Bentley (3), the fall of morphine in fresh latex from 21.8 to 12% is due to atmospheric oxidation. Ramstad (4) has observed that 50% of morphine present in opium undergoes deterioration due to the peroxidase enzyme action. He stated that the morphine content deteriorated from 22% to 11% to 13% in his studies. Results on the deterioration of morphine in fresh latex of Papaver somniferum have been published by Professor Dalev et al. (5).

The present study aims to ascertain whether the fresh latex collected from capsules of Indian opium poppy actually contains 20% morphine and the percentage loss in morphine content during the 24 hours following lancing. Many preservative chemicals, electrolytes, antioxidants and enzymatic deactivators were tested to determine their potential for arresting the deterioration of morphine in fresh latex and findings are reported in this paper.

## MATERIALS AND METHODS

In November 1974 the experimental field of the Government Opium and Alkaloid Works, Neemuch, India, was sown with seed of the poppy varieties Telia (Indian) and Iranian. Lancing of capsules commenced in March 1975. Capsules were lanced during the afternoon and fresh latex collected from their surface one hour after lancing.

The one hour period was necessary to accumulate sufficient latex for the various tests. About 500 to 600 capsules were lanced and latex collected. Morphine content in fresh latex was estimated in the field using a mobile laboratory. A sample of the freshly collected latex was kept as a check under laboratory conditions for 24 hours after which its morphine content was determined.

Fresh latex collected in the field was divided into samples of 8 grammes each. 0.5 gramme of one of the 24 preservative chemicals and control listed below was added to and thoroughly mixed with a sample of the fresh latex. The samples with preservatives and the control were analysed for morphine content the next day.

The fresh latex oozings on the surface of the capsules after one hour following lancing were collected the next morning before 8 a.m. and morphine content estimated.

Morphine percent in fresh latex, latex with added preservatives and oozings was estimated separately for each of the three lancings.

Preservative chemicals investigated to arrest deterioration of morphine in fresh latex include: (1) sodium ascorbate, (2) hydroxylamine hydrochloride, (3) butylated hydroxy toluene, (4) Kalanamak[2/], (5) syrupy phosphoric acid, (6) aniline, (7) potassium fluoride, (8) citric acid, (9) powdered yeast, (10) borax, (11) sodium phosphate, (12) sodium carbonate plus sodium bicarbonate (1:1), (13) formalin, (14) phenol, (15) lead acetate, (16) sodium sulphate, (17) sodium acetate, (18) sodium bicarbonate, (19) calcium chloride, (20) gallic acid, (21) pyrogallic acid, (22) sodium chloride (common salt), (23) sodium carbonate, (24) celin (ascorbic acid) and (25) distilled water.

In two separate experiments, the surface of poppy capsules in the field were smeared with a cotton swab of 5% dispersion of sodium ascorbate in glycerine and 5% aqueous sodium sulphite before lancing. The lancing knives were dipped in the test solutions immediately before lancing the capsules. The glycerine was not satisfactory as a solvent since the fresh latex would not form pellicles and stick to the surface of capsules. The exudate dropped from the capsules on to the leaves below. Also, glycerine contaminated the latex, thereby making accurate estimation of morphine in opium difficult.

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2/ A local product composed of sodium carbonate, sodium chloride, sodium sulphide and sodium sulphate.

In addition to tests in the field of the Government Opium and Alkaloid Works, Neemuch, experiments with selected preservatives were evaluated under actual field conditions at 3 selected farms.

Method of estimation of morphine:

Determination of morphine in the fresh latex and opium samples with preservative chemicals was based on the method laid down in the British Pharmacopoeia, 1963 (6).

pH of the fresh latex:

pH of fresh latex immediately after lancing was estimated at intervals of 30 minutes for a period of 2 hours. Initial and final readings of pH were compared to examine the possible bio-chemical reactions taking place in the latex.

## RESULTS AND DISCUSSION

Results obtained in 13 field experiments on the deterioration of morphine and effects of preservatives in the fresh latex are given in Tables 1 to 5.

Fresh latex from the first lancing contained the highest morphine percent. The variety Telia had the highest morphine content from 14.50% to 16.46% for the varieties tested (Table 1). In all varieties, there was a decrease in morphine content between the fresh latex and oozings collected the next morning. The maximum loss of 5.89 units was observed in the Iranian variety. Oozings showed a morphine content as low as 9.47% compared to the much higher values obtained with fresh latex (Table 1).

There was a definite lowering of morphine percent between the fresh latex of first lancing and that obtained from subsequent lancings (Table 1) (11.52 to 12 % for the second lancing and 9.30 to 10.86 % for the third lancing). The oozings of second lancing had the lowest morphine percent, only 8.62%. Reductions in morphine content in the opium checks stored for 24 hours under laboratory conditions was also observed when compared to values obtained in fresh latex. The observations were similar in all varieties tested. The maximum decrease occurred with the Iranian variety (Table 1).

The effects of preservative chemicals on morphine content in fresh latex of Iranian and Telia varieties are given in Tables 2 and 3. Morphine content in fresh latex of Telia varied from 16.22% to 16.70% for the first lancings. Out of 24 chemicals tested, only phosphoric acid, $Na_2CO_3$+ $NaHCO_3$ (1:1) and phenol showed preservative action. In the latex of second lancing, positive preservative effects are indicated with the addition of phosphoric acid, sodium acetate, sodium chloride and citric acid (Table 3).

For the Iranian variety, sodium ascorbate and hydroxylamine hydrochloride indicated preservation of morphine even in latex from the third lancing (Table 2).

Results obtained from the three selected farmers are given in Table 4. Of the ten chemicals tested, preservative effects were observed only from Kalanamak, phosphoric acid, hydroxylamine hydrochloride, $Na_2CO_3$+$NaHCO_3$, sodium chloride and phenol.

In experiments with chemicals smeared on the surface of capsules with a swab before lancing, loss in morphine could not be arrested with sodium ascorbate and sodium sulphite solutions. Smearing each capsule with a preservative is a cumbersome operation under field conditions. Morphine estimation on dry matter basis was found difficult where sodium ascorbate was smeared since the latex collected was contaminated with glycerine.

## CONCLUSION

The fresh latex collected one hour following lancing has 16.7% morphine for Indian variety Telia. This was the highest morphine content recorded for five varieties in the study. Morphine content in latex exposed to laboratory conditions for 24 hours was lowered by 2.48 units. There was a decrease of 5.8 units in morphine in oozings, indicating the effects of sun and heat following lancing on the deterioration of morphine.

The fresh latex collected had a pH of 6.8 which decreased to 5.0 after two hours. The lower pH indicates the biochemical reactions taking place in the latex when exposed to atmospheric conditions. Reduction in morphine content could be attributed either to its decomposition or partial conversion into other organic compounds.

Of the 24 chemicals used to prevent the deterioration of morphine, six were promising, namely, Kalanamak, sodium chloride, citric acid, sodium acetate, sodium ascorbate and hydroxylamine hydrochloride. Kalanamak is used as a preservative for pickles and has medicinal properties. Sodium sulphide, a constituent of Kalanamak, is a reducing agent and an enzyme poison. Sodium carbonate neutralises the acids produced in the latex and sodium chloride, a strong electrolyte, is an inhibitor of ensymatic action.

Studies with preservatives are being continued to arrive at definite conclusions on their effects in arresting the deterioration of morphine in the latex of Papaver somniferum.

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REFERENCES

(1) Vorozhtsov, N.N. and Troshchenko, A.T. "Der Morphingehalt in Milchsafte des Opium Mohns" Comptes Rendus de l'Académie des Sciences de l'Union des Républiques socialistes soviétiques 1935, (2) 555-558 (In Russian; German Summary 558); Nilov, V.I., Nilova W.P. and Troshchenko, A.T., "Fermentative Oxidation of Morphine in the latex of the Opium Poppy" Biokhimiyal, 165-82 (1936); Chemical Abstracts 30,7779.

(2) Fulton, C.C. "The Opium Poppy and other Poppies", U.S. Treasury Department, Bureau of Narcotics, Washington D.C., 1944, 29.

(3) Bentley, K.W., "The Chemistry of the Morphine Alkaloids" Clarendon Press, Oxford, 1954, 15.

(4) Ramstad, E., Modern Pharmacognosy, McGraw Hill Book Company Inc., New York, 1959, 343, 344, 407.

(5) Dalev, D., et al., Bulletin on Narcotics, XII, (1) (1960), 25.

(6) British Pharmacopoeia, 1963, 544.

TABLE 1

MORPHINE CONTENT IN FRESH LATEX AND OPIUM

| Location: | Opium Factory Neemuch | Opium Factory Neemuch | Laxmipura (Rajasthan) | Bharukheda (M.P.) | Khadavda (M.P.) | Opium Factory Neemuch | Opium Factory Neemuch | Opium Factory Neemuch | Opium Factory Neemuch |
|---|---|---|---|---|---|---|---|---|---|
| Variety: | Iranian | Telia | Dhaturia | Ranjhatak | Kanta Telia | Telia | Iranian | Telia | Iranian |
| Temperature °C | | | | | | | | | |
| (i) field morning 7 a.m. | 20 | 20 | 21 | 20 | 20 | 20 | 20 | 20 | 20 |
| (ii) field midday | 33 | 33 | 33 | 33 | 34 | 34 | 34 | 34 | 34 |
| (iii) laboratory midday | 28 | 28 | 27 | 30 | 29 | 30 | 30 | 28 | 28 |
| Relative humidity: % | 48 | 48 | 43 | 44 | 44 | 43 | 43 | 44 | 44 |
| Date of lancing: | 10.3.75 | 10.3.75 | 13.3.75 | 14.3.75 | 15.3.75 | 11.3.75 | 12.3.75 | 13.3.75 | 14.3.75 |
| Number of lancing: | First | | | | | Second | | Third | |
| | Anhydrous Morphine on dry matter | | | | | Anhydrous morphine on dry matter | | Anhydrous morphine on dry matter | |
| | % | % | % | % | % | % | % | % | % |
| Fresh latex analysed immediately | 16.43 | 16.46 | 16.40 | 14.50 | 15.50 | 11.52 | 12.00 | 10.86 | 9.30 |
| Latex analysed after keeping in the laboratory for 24 hrs. | 13.95 | 15.68 | 15.30 | 13.69 | - | 9.87 | 11.36 | 10.41 | 8.83 |
| Oozings, collected next morning and analysed the same day. | 10.60 | 14.79 | 10.99 | 9.47 | 13.25 | 9.49 | 8.62 | - | - |

TABLE 2

EFFECT OF PRESERVATIVES ON MORPHINE CONTENT

Location: Field in Government Opium Factory, Neemuch (M.P.)

Variety: Iranian

| | | | |
|---|---|---|---|
| Temperature °C | | | |
| (i) Field | 33 | 33 | 34 |
| (ii) Laboratory | 28 | 28 | 28 |
| Date of lancing: | 10.3.75 | 12.3.75 | 14.3.75 |
| Number of lancing: | | | |

| Treatments | Morphine content on dry matter basis | | |
|---|---|---|---|
| | % | % | % |
| Opium without preservative as check sample | 13.95 | 11.36 | 8.83 |
| Opium + 0.5g hydroxylamine hydrochloride + 1 ml water | 14.61 | - | 8.72 |
| Opium + 0.5g of sodium ascorbate + 1 ml water | 14.21 | - | 9.13 |
| Opium + 0.5g of $CaCl_2$ + 1 ml water | - | 10.55 | - |
| Opium + 0.5g of KF + 1 ml water | - | - | 8.72 |
| Opium + 0.5g gallic acid | - | - | 8.77 |
| Fresh latex analysed immediately | 16.43 | 12.0 | 9.30 |

TABLE 3

EFFECT OF PRESERVATIVES ON MORPHINE CONTENT

Location: Field in Government Opium Factory, Neemuch (M.P.)

Variety: Telia

Temperature Field °C 33-34

Temperature Laboratory °C 28-30

| Date of lancing: | 10.3.75 | 11.3.75 | 13.3.75 | 15.3.75 |
|---|---|---|---|---|
| Number of lancing: | First | | Second | Third |
| Treatments | Morphine percent on dry matter | | | |
| 1. Opium without preservative as check sample | 15.93 | 15.43 | 9.87 | 10.41 |
| 2. Opium + 0.5g B.H.T. | 12.26 | - | - | - |
| 3. Opium + 0.5g Kalanamak | 15.25 | - | - | - |
| 4. Opium + 11 drops phosphoric acid | 16.06 | - | 11.70 | - |
| 5. Opium + 11 drops aniline | 13.64 | - | - | - |
| 6. Opium + 0.5g KF | 15.09 | - | - | - |
| 7. Opium + 0.5g citric acid + 1 ml water | 15.31 | - | 11.25 | - |
| 8. Opium + 0.5g yeast | 13.86 | - | - | - |
| 9. Opium + 0.5g borax | 12.50 | - | - | - |
| 10. Opium + 0.5g sodium phosphate | - | 8.59 | - | - |
| 11. Opium + 0.5g $Na_2CO_3$ + $NaHCO_3$ (1:1) | - | 16.15 | - | - |
| 12. Opium + formalin (30%) 25 drops | - | 12.60 | - | - |
| 13. Opium + 0.5g ml phenol | - | 15.91 | - | - |
| 14. Opium + 0.5g lead acetate + 1 ml water | - | 14.94 | - | - |
| 15. Opium + 0.5g sodium sulphite + 1 ml water | - | 14.06 | - | - |
| 16. Opium + 0.5g sodium acetate + 1 ml water | - | 15.03 | 11.57 | - |
| 17. Opium + 0.5g $NaHCO_3$ + 1 ml water | - | 14.55 | - | - |
| 18. Opium + 0.5g gallic acid | - | - | 7.86 | - |
| 19. Opium + 0.5g pyrogallic acid | - | - | 7.57 | - |
| 20. Opium + 0.5g NaCl + 1 ml water | - | - | 11.57 | - |
| 21. Opium + 0.5g $Na_2CO_3$+ 1 ml water | - | - | 10.69 | - |
| 22. Fresh opium latex analysed immediately on collection | 16.70 | 16.22 | 11.52 | 10.86 |

TABLE 4

EFFECT OF PRESERVATIVES ON MORPHINE CONTENT

| Name of village and State: | Lakshmipura (Rajasthan) | Bharukheda (Madhya Pradesh) | Khadavda (M.P.) |
|---|---|---|---|
| Variety: | Dhaturia | Ranjhatak | Kanta Telia |
| Temperature Field °C | 33 | 33 | 34 |
| Temperature Laboratory °C | 27 | 30 | 29 |
| Date of lancing: | 13.3.75 | 14.3.75 | 15.3.75 |
| Treatments | Morphine percent on dry matter | | |
| 1. Opium + 11 drops $H_3PO_4$ | 15.58 | - | 14.43 |
| 2. Opium + 0.5g citric acid | 14.96 | - | 14.69 |
| 3. Opium + 0.5g Kalanamak | 16.39 | - | 15.19 |
| 4. Opium + 0.5g hydroxylamine hydrochloride | 14.96 | - | - |
| 5. Opium + 0.5g $Na_2CO_3$ + $NaHCO_3$ 1:1 + 1 ml water | - | 14.31 | - |
| 6. Opium + 11 drops phenol | - | 14.26 | - |
| 7. Opium + 0.5g lead acetate + 1 ml water | - | 13.36 | - |
| 8. Opium + 0.5g sodium acetate | - | 13.89 | 14.21 |
| 9. Opium + 0.5g celin (Vitamin C) | - | - | 14.85 |
| 10. Opium + 0.5g NaCl | - | - | 15.25 |
| 11. Opium + 60 ml distilled water | - | - | 15.11 |
| 12. Opium without preservative as check sample | 15.30 | 13.69 | - |
| 13. Fresh opium latex analysed immediately after collection | 16.40 | 14.50 | 15.50 |

TABLE 5

PRESERVATIVE EFFECT OF SODIUM ASCORBATE AND SODIUM SULPHITE

Location: Government Opium Factory, Neemuch (M.P.)

Variety: Telia

Temperature °C

(i) Field 33.5

(ii) Laboratory 29.0

Relative humidity:

Field percent 43

Date of lancing: 12.3.75 13.3.75

Number of lancing: First First

Anhydrous morphine percent on dry matter

| Treatments | Capsules smeared with 5% dispersion of | | |
|---|---|---|---|
| | Sodium ascorbate | Sodium sulphite | Check |
| 1. Fresh latex | 16.14 | 11.46 | 16.46 |
| 2. Opium without preservative kept for 24 hrs | - | 11.66 | 15.68 |
| 3. Opium + 0.5g sodium ascorbate | 15.00 | - | - |
| 4. Oozings | 8.83 | 10.28 | 14.79 |